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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,294	12/28/2001	Jean Marie Vogel	9676-311	2836

20582 7590 03/24/2004

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,294	VOGEL ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-16,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8-16, 19, 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Amendment, Response/Arguments and the request for extension of time (3 months- granted), all filed 11/19/03 is acknowledged.

Claims 1-4, 8-16, 19 and 20 are pending. The Title has been amended as requested. Claims 5-7, 17 and 18 have been cancelled (based on non-elected subject matter). Claims 1-4, 8-16, 19 and 20 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 8-16, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajagopalan *et al.* (US Pat. No. 5,843,987) in view of Boschetti *et al.* (US Pat. No. 5,635,215).

Rajagopalan teaches a method for treating gastroesophageal reflux disease (GERD), which comprises parenterally administering particles of ellagic acid, which is known to be useful for the treatment of gastrointestinal disorders, such as GERD, to a

human or other animal (see reference column 1, lines 1-18); (col. 2, lines 21-57); (col. 5, lines 15-42); examples and claims.

According to Rajagopalan, ellagic acid has prokinetic activity, and therefore stimulates motility of the gastrointestinal tract, enhances esophageal contractility, gastric emptying and small intestine transit time. Furthermore, ellagic acid is useful in the treatment of constipation, heartburn, non-ulcer esophagitis, GERD, esophagitis, gastric ulcers, and/or duodenal ulcers (col. 2, lines 25-35).

The method of treatment can be accomplished by administration of ellagic acid in various suitable unitary dosage forms, such as orally, parenterally, or rectally. Oral liquid dosage forms include suspensions, syrups, elixirs and solutions. Solid dosage forms include powders, pills, compressed tablets, hard capsules containing beads or particles of ellagic acid or soft gelatin capsules. Oral dosage forms can also be film coated. For parenteral dosage forms, acceptable carriers include sterile water, saline solution, glucose solution or mixtures of saline and glucose solutions (col. 5, lines 26-42).

The examples at columns 10-12 demonstrate various dosage forms, such as oral solutions, suspensions and parenteral solutions. Example 5 demonstrates the teaching of a parenteral solution of ellagic acid in combination with propylene glycol, chlorocresol and water for injection.

What is lacking in Rajagopalan is collagen (or a derivative thereof) or glucosaminoglycans as the particular coating material of the microparticles.

Boschetti ('215) teaches microspheres and injectable solutions comprising a hydrophilic copolymer coated with a cell adhesion promoter, wherein different types of cell adhesion promoters, include, collagen, gelatin, glucosaminoglycans, lectins, polycations, or any other synthetic biological cell adhesion agent and wherein the presence of a cationic charge on the surface of the microspheres makes it possible to initiate and improve cell adhesion (see reference column 1, line 46 through col. 2, line 42).

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use hydrophilic copolymer coatings, that are coated with cell adhesion agents (i.e., collagen, glucosaminoglycans) as taught by Boschetti with the injectable particles of Rajagopalan because Boschetti teaches that the microspheres hydrophilic character enables them to be placed in suspension, without formation of aggregates nor adhesion to the walls of the catheters, syringes, needles and other materials used in embolization and similarly Rajagopalan teaches parenteral administration of particles, specifically of ellagic acid for the treatment of gastrointestinal reflux disease. The expected result would be a hydrophilic-coated formulation comprising injectable particles for the treatment of various gastrointestinal disorders.

Regarding the administration of the microparticles into the lower esophageal sphincter or diaphragm, the prior art (Rajagopalan) teaches parenteral administration of particles into the gastrointestinal tract. The gastrointestinal tract as used therein, includes the entire digestive tract, including the esophagus, stomach, small intestine,

large intestine, and the colon (see col. 4, lines 64-67). Furthermore, one of ordinary skill in the pharmaceutical art could determine a suitable means and route of administration based on the intended locality of treatment. There is no criticality seen in the particular area of administration since the prior art teaches the administration of particles into the gastrointestinal tract for the treatment of gastro-related diseases.

Response to Arguments

Applicant's arguments filed 11/19/03 have been fully considered but they are not persuasive.

The Applicant argues regarding the rejection of Claims 1-4, 8-16, 19 and 20 over Rajagopalan et al. (US '987) in view of Boschetti et al. (US '215) stating, "Rajagopalan discloses a method of stimulating gastrointestinal ("GI") motility with ellagic acid. Rajagopalan alleges that ellagic acid has prokinetic activity, and therefore, stimulates motility of the gastrointestinal tract (GI) and is useful in the treatment of gastroesophageal reflux disease (GERD)....ellagic acid exhibits these effects perorally despite the fact that it is poorly absorbed from the GI tract. However, there is no disclosure or suggestion in Rajagopalan of a method of treating GERD through tissue bulking or tissue bulking by administration of biocompatible hydrophilic microparticles into the lower esophageal sphincter or the diaphragm as presently claimed. Rajagopalan is totally silent regarding any method of tissue bulking and only concerns the treatment of GI disorders by using a drug, *i.e.,* ellagic acid that allegedly affects the motility of the GI tract. There is no disclosure or suggestion whatsoever in Rajagopalan that the solid dosage forms could be used as implants for tissue bulking. Although Rajagopalan generally

discloses that ellagic acid can be formulated into solutions for parenteral administration, there is no indication that the parenteral administration disclosed therein has anything to do with tissue bulking, as presently claimed."

These arguments have been fully considered, but are not found to be persuasive. The Applicants' argument that there is no disclosure or suggestion and that Rajagopalan are totally silent with regard to a method of treating GERD through tissue bulking or tissue bulking by administration of biocompatible hydrophilic microparticles into the lower esophageal sphincter or the diaphragm as presently claimed is not persuasive, since the prior art teaches the same method of treatment for a similar disease as that instantly claimed, gastroesophageal reflux disease or simply GERD, by parenteral means and the Applicants have not demonstrated that the amounts taught by the prior art are not tissue-bulking amounts as instantly claimed. Moreover, with respect to "tissue-bulking amounts" as presently claimed, the term is a functional expression with no specific units disclosed. It is unclear as to the precise amount or extent to which a 'tissue-bulking amount' is consisted of. The prior art teaches suitable and effective amounts of ellagic acid to treat gastrointestinal disorders.

Secondly, the Applicant argues, "Boschetti fails to remedy the deficiencies of Rajagopalan. Boschetti disclose a microsphere comprising a hydrophilic acrylic copolymer coated with a cell adhesion promoter and a marking agent useful for embolization, i.e., therapeutic vascular occlusion. Boschetti do not disclose or suggest a method of treating GERD by tissue bulking, nor the administration of microparticles into the lower esophageal sphincter or diaphragm. Boschetti is silent with regard to any method of tissue bulking. The Examiner has failed to establish a *prima facie* case of obviousness. One of ordinary skill in the

art would not have been motivated to modify or combine the teaching of Rajagopalan and Boschetti because the references are directed to different fields of treatment, use of different materials and approaches. There was no suggestion of desirability to combine the references at the time of the invention to achieve the presently claimed invention. The microspheres for vascular occlusion as disclosed in Boschetti can hardly be combined with the use of a GI motility drug of Rajagopalan to achieve the present invention's method of treating GERD by tissue bulking. Neither reference discloses or suggests any method of tissue bulking, not to mention the specific method of administering biocompatible hydrophilic microparticles into the lower esophageal sphincter or diaphragm, as presently claimed."

These arguments are not found to be persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Rajagopalan teach a method for treating gastroesophageal reflux disease (GERD), which comprises parenterally administering particles of ellagic acid. Rajagopalan was lacking in the sense that they do not explicitly teach that the microparticles are coated with or linked to collagen, or derivative thereof, or glucosaminoglycans or mixtures thereof. The secondary reference of Boschetti was relied upon for the teaching of the obviousness of employing microspheres and injectable solutions whereby the hydrophilic particles are coated with cell adhesion

promoters (i.e., collagen, glucosaminoglycans), such as instantly claimed. The Applicant's argument that Boschetti is silent with regard to any method of tissue bulking was also not found to be persuasive since, as pointed out above with regard to Rajagopalan, Applicants have not demonstrated that the amounts taught by the prior art are not tissue-bulking amounts. Moreover, in Applicant's specification, at page 17, lines 10-16, Applicants disclose "Microparticles of the present invention which have the specific properties of cell adhesion and growth promotion can be used directly for tissue bulking." Keeping this in mind, the formulation of Boschetti, which also comprises microspheres and injectable solutions wherein the hydrophilic polymers are coated with *cell adhesion promoters*, could also be used for tissue bulking since the microparticles of Boschetti would also have the same cell adhesion properties and therefore could be used directly for tissue bulking, as similarly desired by the Applicants. Moreover, with respect to "therapeutically effective tissue-bulking amount of hydrophilic microparticles" as presently claimed, the term is a functional expression with no specific units disclosed. It is unclear as to exactly how much a 'tissue-bulking' amount is. The applicants have not thoroughly demonstrated any tissue-bulking amounts. The prior art recognizes treating gastrointestinal disorders through the parenteral administration of hydrophilic particles and cell adhesion promoters. Therefore, since, the prior art combinations provide for similar ingredients and methods for treating the same disease (GERD) as the applicants, a *prima facie* case of obviousness has been clearly established. Hence, the instant invention is rendered obvious and unpatentable over the prior art of record.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

hns
March 18, 2004

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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